

Virtual reality for interactive binocular treatment of amblyopia

P E Waddingham^{1,2}, S V Cobb¹ R M Eastgate¹ and R M Gregson²

¹VIRART, School of M3, University of Nottingham,
University Park, Nottingham, Nottinghamshire, UK

²Directorate of Ophthalmology, Nottingham University Hospital NHS Trust Queens Campus,
Derby Road, Nottingham, Nottinghamshire, UK

¹*epxpes@nottingham.ac.uk, sue.cobb@nottingham.ac.uk,
richard.eastgate@nottingham.ac.uk, richard.gregson@nuh.nhs.uk*

www.virart.nott.ac.uk/ibit

ABSTRACT

Amblyopia, or 'lazy eye', is currently treated by wearing an adhesive patch over the non-amblyopic eye for several hours per day, over a period of many months. Non-compliance with patch wearing is a significant problem. Our multi-disciplinary team involved clinicians and technologists to investigate the application of VR technology in a novel way. We devised a binocular treatment system in which children watch a video clip of a cartoon on a virtual TV screen, followed by playing an interactive computer game to improve their vision. So far the system has been used to treat 39 children of which 87% have shown some improvement in vision. Vision improvement tended to occur within the first 3-4 treatment sessions. This paper describes research development of the I-BiT™ system. We present a summary of results from clinical case studies conducted to date and discuss the implications of these findings with regard to future treatment of amblyopia.

1. WHAT IS AMBLYOPIA?

Amblyopia, or 'lazy eye', is reduced corrected visual acuity which exists in the absence of any detectable organic disease. Amblyopia can be the result of a squint (strabismic amblyopia), in which both eyes are not straight, a difference of the refractive state of each eye (anisometropic amblyopia) or the result of both squint and refractive inequality (mixed amblyopia, combined anisometropic and strabismic amblyopia), in which there is a squint as well as a stronger corrective glasses lens for one eye. This condition affects 2-5% of the population (Hillis, 1986; Thompson et al., 1991) and is currently treated by wearing an adhesive patch over the non-amblyopic eye for several hours per day, over a period of many months (Cleary, 2000). Although this form of occlusion therapy is successful, success rates are variable (Hiscox et al., 1992) and non-compliance with patch wearing is a problem that can result in unsuccessful treatment (Louden, Polling and Simonsz, 2002).

Standard teaching has been that amblyopia caused by strabismus and anisometropia should be treated before a child is 7 years of age (von Nooden and Crawford, 1979) and research studies have found that screening at a younger age (i.e. under 3 years) leads to better treatment outcomes (Williams et al., 2003). Children who are not successfully treated within this critical period will be left to cope with their condition into adulthood. Whilst, not disabling in itself, having one weak eye can prohibit people from some occupations such as those driving professions which require a HGV licence, the police force and ambulance driver, and there is also a higher risk of losing the good eye in later life due to injury or eye disease. The UK visually impaired register consists of large numbers of people who are amblyopic, but have lost their remaining 'good' eye through injury or disease (Rahi et al., 2002; Tommila and Tarkkanen, 1981).

2. INTERACTIVE BINOCULAR TREATMENT

A research collaboration between orthoptists, ophthalmologists and the virtual reality applications research team (VIRART) examined the potential application of VR technology to treatment of amblyopia. Our multi-disciplinary team considered how the features of VR could be used to provide a new way to treat amblyopia that young children would find interesting and so encourage them to comply with treatment. Together we

devised a novel system providing interactive binocular treatment for amblyopia; the I-BiT™ system (Eastgate et al., 2006).

The basis of this new approach for amblyopia treatment is preferential stimulation of the amblyopic eye, achieved by presenting separate (but visually related) images, one to each eye independently. It was initially considered that this treatment may be more effective than patching occlusion merely due to treatment compliance; our expectation was that young children would find it more attractive to watch cartoons and play computer games than wearing an eye patch and so they would be prepared to follow a course of treatment. At the project outset, we had no indication as to how much treatment would be needed. Patching occlusion therapy can take up to 400 hours of treatment in total (Cleary, 2000).

One assumes that prolonged patching treatment is required as time is required for cell growth and ‘neural wiring’ of receptor cells for the amblyopic eye. However, the neurology underlying the human conditions of strabismus and amblyopia remains elusive (Barrett et al., 2004). If vision is blurred or one eye is covered during the critical period in postnatal development, neurons in the visual cortex lose their responses to stimulation through that eye within a few days. Anatomical changes in the nerve terminals that provide input to the visual cortex have previously been observed only after weeks of deprivation, suggesting that synapses become physiologically ineffective before the branches on which they sit are withdrawn. (Antonini and Stryker, 1999). So if adequate stimulation is lacking during a critical or sensitive period in early childhood, certain cortical functions such as sight will never develop properly later on (Sengpiel, 2005).

Furthermore, we were uncertain regarding which conditions I-BiT™ treatment would be most suitable for. We were not even sure that children with very poor vision in the amblyopic eye would be able to see what was on the computer screen at all as the brain tends to suppress or disregard the content seen by the amblyopic eye. Standard orthoptic tests demonstrate suppression in most children with dense amblyopia (very poor vision) (Waddingham. Personal communication).

3. WHY VIRTUAL REALITY?

Virtual Reality systems comprise computer generated virtual environments which may be representations of real world environments, simulated or abstract environments (e.g. Ellis, 1994). When using a VR system, a stereo image is perceived as a result of viewing two images of the same scene, one presented to each eye, at slightly offset viewing angles which correspond to the different viewpoints our left and right eyes get when viewing the real world. This stereo effect is intended to produce a sensation of depth; of seeing the virtual environment in 3D and therefore perceiving it as a “virtual world”. This sensation is further enhanced by viewing the virtual environment via an immersive display such as a head-mounted display (HMD) or CAVE system.

It was this aspect of VR that was important for amblyopia treatment. The basis of the I-BiT™ system was that we could present an image separately to each eye. Not for the purpose of providing a stereo image, but as a means of presenting different visual content to each eye, in which at least one of the images includes dynamic stimuli. This is illustrated in Figure 1., showing a fish tank constructed in an empty Superscape® 3D environment. The basic principle is that the amblyopic or lazy eye is shown the interesting bit (the fish), whilst the good eye is shown the less interesting bit (the background). When viewed through a stereo viewer the patient should see the fish in the tank. Therefore, the amblyopic eye received preferential visual information. To make sure that the patient can fuse the image (line the two images up correctly) there are a significant number of elements (the base of the tank and the plants) common to both images.

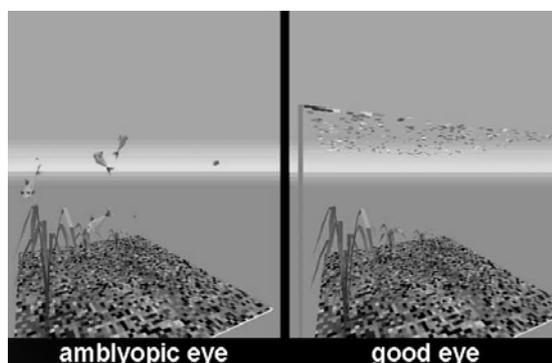


Figure 1. Different visual information is presented to each eye.

It was considered that VR could be used for I-BiT™ presentation because it offers;

- Control over the content, resolution and contrast of images presented to each eye
- Control over the visual angle to compensate for any deviation of the eyes and IPD

4. SELECTING A SUITABLE DISPLAY DEVICE

A desktop computer alone does not provide a 3D experience unless attached to a head mounted display (HMD) or an alternative display to provide a 3D effect. We needed to find a 3D viewer that would be suitable for children in the range 5 to 8 years of age. HMDs such as the Virtual Research V8 were too heavy for extended use by our expected user population and children found the headset too claustrophobic. The centre of gravity is at the front which pulls the headset forward, causing neck strain. In addition the interpupillary distance (IPD the distance between the two pupils) did not go down to small enough levels for children.

The Cy-Visor DH-4400 binocular headset, although not designed specifically for children, is much more lightweight than the V8, it has a less enclosed design the IPD was small enough for the children we tested. However, although the Cy-Visor could be worn for 30 minutes of treatment, it needed to be held in place by the clinician whilst the child was slightly reclined on the seat.

We decided that we needed to develop our own display in order to conduct preliminary case study trials. The system we developed incorporated a device called a Cyberscope (Wired, 1993). A cyberscope is a plastic hood which fits onto the front of the 15" PC monitor to allow it to be used as a stereo display. This device uses a combination of mirrors to take the image from a standard monitor and present one half of it to one eye and one to the other eye. The monitor display is divided vertically down the middle, and in each half the image to one of the eyes is displayed rotated through 90° to give the images the desired proportions. The mirrors in the Cyberscope rotate the images back the right way up and send them, one to each eye (as illustrated in Figure 2). In this example, both eyes are presented with an image of the clock surround. The left eye is also presented the clock numbers whilst the right eye is presented with the clock hands. Only by using each eye can the patient see what time is shown on the clock.

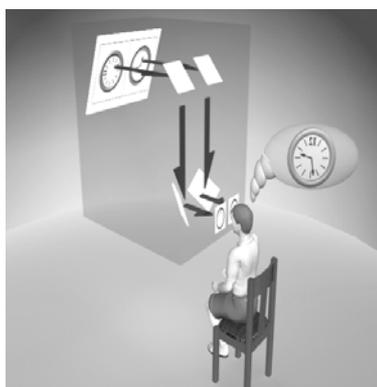


Figure 2. *Concept of the desk mounted display, showing different images presented to each eye.*

By using an LCD monitor we could make the entire display system small and light enough to be fitted into one box. The box was designed such that, when placed on a standard desktop, and used in conjunction with an adjustable chair, the viewing holes are at a height suitable for children.

As the visual scene was visible only to the patient, we needed to provide a secondary screen display for the clinician so that they could see what the patient was doing and check that they were attending to the display with both eyes. This secondary display was also used as the practitioner's control interface, allowing clinicians to select content of the patient's display and configure software adjustments for:

- the viewing angle to each eye
- calibration of IPD
- selecting which eye is the amblyopic eye and which is the non-amblyopic eye
- These controls are described in more detail in (Eastgate et al., 2006).

Figure 3 shows the research prototype system in use.



Figure 3. Desk mounted version, showing child looking through cyberscope and clinician PC.

5. SOFTWARE DEVELOPMENT

The virtual environment needed to be capable of presenting less detail to the non-lazy eye and more to the lazy one. Thus, two versions of each virtual environment were built; one containing visually rich and dynamic objects and the other containing static and less interesting objects.

Two games were developed for the first version of the system. A virtual maze game based on the popular 1970's pac-man arcade game (see Figure 4) and a racing game (Figure 5). Pac-man appeared to be ideal for the I-BiT™ system as the game content is comprised of different components: a central character that must navigate around a maze avoiding the “ghosts”, whilst attempting to collect all the yellow “dots”. The first decision to be made was regarding the level of detail to be displayed in each eye. Essentially there are two distinct groups of components in the game; objects that move and objects that do not. As a result of this, the design decision was to have one eye see the pac-man character and ghosts, whilst the other saw the maze and yellow dots. Also, in order to ensure that the difference was not too great, some continuity between the two was incorporated, in this instance, some elements of the maze were included within the image containing the moveable objects.

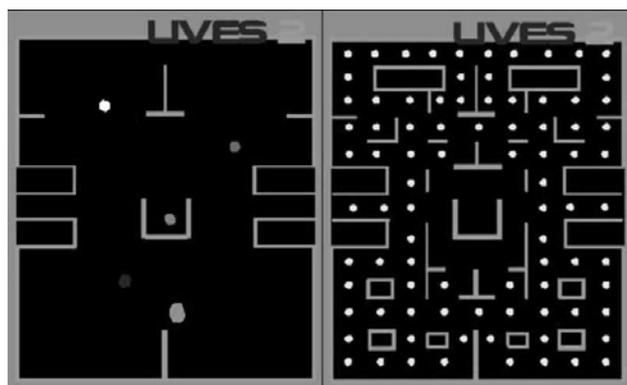


Figure 4. The virtual pac-man game.

Although pac-man seemed an ideal game choice, offering a simple game to construct that is easy to understand and gender non-specific, in our trial studies children did not find the game exciting and interesting to play. They complained of limited motion, limited routes around the course, too many ghosts moving in all different directions. It was easy to get trapped and then eliminated by the ‘ghosts’, which meant that the game wins more often than the child. There was no facility to record performance timings or achieve a score and so the children were not motivated to continue playing the game.

Figure 5. shows the racing game (version 2 with additional icons). In order to get the child to focus on the game, each eye was presented with half a target and alternating white lines in the centre of the road. This

meant that one eye sees a white line, whilst the other eye sees the next white line, therefore combined, it looks like a continuous flow. Some features of the track were presented to both eyes and features of the surrounding environment were presented to each eye separately. The patient had to drive around the track and try to collect the target icons. At the end of the game the number of icons collected and laptime were displayed. This encouraged children to continue playing the game to improve their score. An equal number of icons were presented to each eye and the performance score from each eye was displayed on the clinician's screen. This enabled the clinician to determine whether the amblyopic eye was being used.

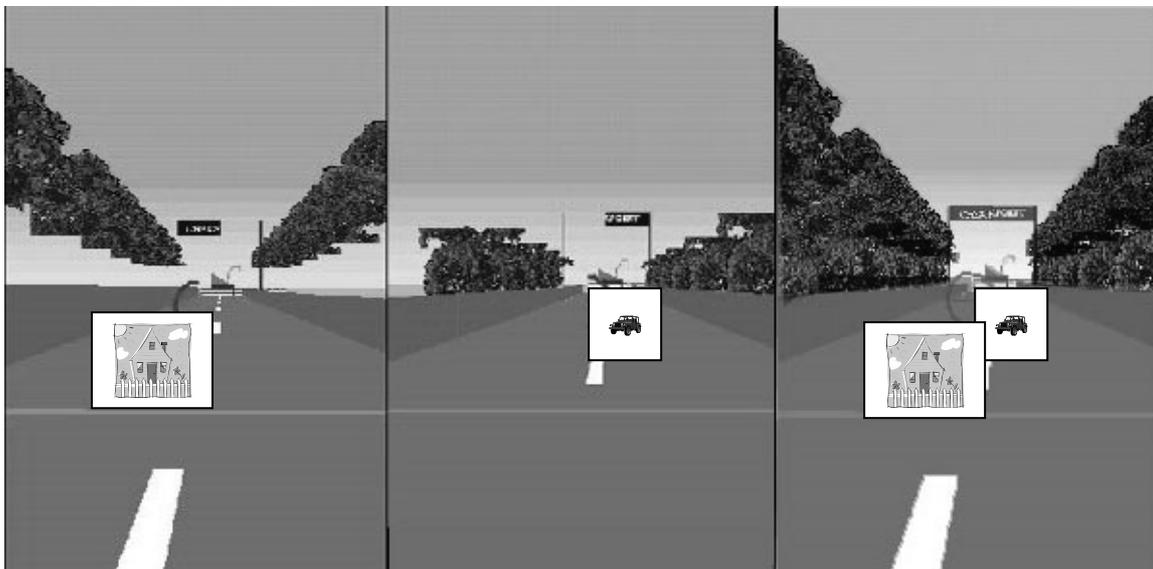


Figure 5. *The racing game as presented to the left eye, the right and the composite view of both images.*

These games were not sufficient to maintain the childrens' interest for continuous play of more than 10 minutes. As we required 30 minutes visual treatment for each session, the system was adapted such that we could present video images via the virtual environment. A virtual TV screen was constructed and video content was presented to the amblyopic eye only. The periphery of the TV surround was presented to both eyes to allow fusion and binocular viewing to occur. A selection of 20-min video clips were available for the children to choose from.

6. CLINICAL CASE STUDIES

We have conducted a number of studies to assess suitability of the I-BiT™ system as a viable treatment of amblyopia. These studies have examined different aspects system design and use. Table 1 presents a summary of clinical case studies conducted to date. These were conducted at two sites by two clinical research teams; the orthoptic unit at Queens Medical Centre, Nottingham and the orthoptic unit at Gartnavel Hospital, Glasgow. Studies are represented using a number system as follows:

- [1] Usability and acceptance of the system by patients, parents and clinicians
- [2] Nottingham studies:
 - [2a] Pilot study, proof of concept using cyberscope desktop viewer, assessment of I-BiT™ system as a treatment for those children who were occlusion treatment failures and children who required occlusion treatment but refused to start the therapy (Waddingham et al., 2006)
 - [2b] Pilot study, single case study using Cy-Visor headset
 - [2c] Follow-on study, effectiveness of the I-BiT™ system as a primary treatment using the desk mounted version (Waddingham et al., in preparation)
- [3] Glasgow studies:
 - [3a] Single case study, same experimental design as study 2b, with the addition of VEP measurement
 - [3b] Follow-on study, effectiveness of using Cy-Visor system as a secondary treatment (Cleary et al., submitted)

Patient composition and trial conditions for each study are listed in Table 1. Performance measures varied according to the study requirements. The usability study consisted of a questionnaire-based assessment for

both child and parent and demonstration of the system to children and clinicians. Feedback from this study fed into the pilot studies. In studies 2a, 2b, 3a and 3b visual acuity (VA) was measured before and after each treatment session using LogMAR Glasgow Acuity Cards (McGraw, Winn 1993). In studies 2c and 2d VA was only measured at the end of the treatment session as examination of the data from the previous studies did not show any great variation in vision pre and post session and added another 10 minutes to the session time. The Glasgow Acuity Cards measure visual acuity in consistent gradation from 6/38 to 6/3 at 3 metres testing distance. The patient is shown a flip chart card, which has 4 letters per line. Debate exists to what is considered a significant improvement in vision but for logMAR charts it has been suggested that a change of 0.200 log units (2 lines or 8 letters on the vision test we used) should be used to ensure a real change has occurred (Stewart, 2004) For this reason, change in visual acuity is also presented in terms of percentage proportional improvement (Stewart et al 2003). This measures the changes in vision from the start of treatment to the end of treatment for each eye and is more meaningful to patients (and parents). Visual Evoked Potentials (VEPs) is a method of measuring the electrical responses of the visual part of the brain to visual stimulation and is applied as an objective measure of vision.

Table 1. Summary of clinical case studies using I-BiT™ system for amblyopia treatment.

Study and patient groups	Trial conditions	Results
[1] Usability study (Nottingham). 15 Children waiting for a paediatric clinic were asked to participate. 4 sessions	<ul style="list-style-type: none"> ▪ Cyberscope desk-viewer ▪ Games and video clip 	<ul style="list-style-type: none"> ▪ Easy to use and very well liked by children. ▪ More activities are required within the system to maintain children's interest over numerous repeated sessions.
[2a] Preliminary pilot study (Nottingham) to determine effectiveness for amblyopia treatment <ul style="list-style-type: none"> ▪ 6 children aged between 5-7. ▪ 3 treatment failures, 3 treatment refusers 	<ul style="list-style-type: none"> ▪ Cyberscope desk-viewer ▪ 2-3 sessions per week for 6 weeks ▪ 20 min cartoons + ▪ 10 min VR game (choice of 2 games) 	<ul style="list-style-type: none"> ▪ Significant improvement in VA (average increase 13 letters on LogMAR Glasgow cards) in 5/6 children. ▪ Mean increase = 10 letters ▪ Plateau at session 8 ▪ 3/5 children have maintained or improved on the final VA (11-19 months follow up). 1/5 had atropine with further significant improvement. ▪ Ave. 42% proportional improvement (range 14%-92%)
[2b] Single case evaluation to compare headset with desk-viewer. One 9-year old girl	<ul style="list-style-type: none"> ▪ Cy-Visor Headset ▪ 4 times a week for 2 weeks (8 sessions) 	<ul style="list-style-type: none"> ▪ Dramatic improvement of 13 letters. 8 letters after session 2 ▪ Ave. 32% proportional improvement
[3a] Single case evaluation to compare VA results with VEPs. (Glasgow)	<ul style="list-style-type: none"> ▪ Cy-Visor Headset ▪ Daily session for 5 days: ▪ 30 min I-BiT + ▪ 40 min VEP 	<ul style="list-style-type: none"> ▪ VEP results did corroborate VA. ▪ Study not well tolerated by patient as each session took 1.5 hours to complete ▪ VA increased up to session 4
[3b] Treatment study (Glasgow) to determine effectiveness as a secondary treatment of amblyopia <ul style="list-style-type: none"> ▪ 12 children aged 6-10 ▪ All treatment failures or refusers 	<ul style="list-style-type: none"> ▪ Cy-Visor Headset ▪ Weekly sessions over 12 weeks: ▪ 20 min I-BiT video ▪ 5 min I-BiT game 	<ul style="list-style-type: none"> ▪ Significant improvement in VA in 11/12 children ▪ Improvement ranged 4-15 letters ▪ 2 children VA came up to 6/6 ▪ Significant improvement occurred within 2-3 sessions of treatment ▪ Ave. 35% proportional improvement
[2c] Treatment study (Nottingham) to determine effectiveness as a primary treatment of amblyopia <ul style="list-style-type: none"> ▪ 19 children aged 4-10 years ▪ No previous treatment for amblyopia 	<ul style="list-style-type: none"> ▪ Cyberscope desk-viewer ▪ Weekly sessions over 12 weeks: ▪ 25 min I-BiT video ▪ 5 min I-BiT game ▪ 40 min VEP (at visit 1, 6 & 12) 	<ul style="list-style-type: none"> ▪ 17/19 improved vision ▪ Improvement range 2-20 letters (average 7.8 letters) ▪ Most improvement within first 4 sessions ▪ No correlation VEP with VA ▪ Poor patient tolerance of VEP ▪ Ave. 34% proportional improvement (range 11%-67%)

7. RESULTS

Study [1] assessed usability and acceptance of the system by patients (i.e. children), parents and clinicians. The outcome of this study showed high levels of interest in using the system. Patients preferred this option to receiving occlusion treatment at home and parents said that they would be prepared to have regular visits to the clinic for their children to receive I-BiT™ treatment. Clinicians were also positive about the concept of I-BiT™, although expressed some concerns over the need for additional clinic visits for patients, increasing clinician workload and patient waiting times.

The Nottingham studies [2] were all conducted using the cyberscope desktop viewer. The first pilot study conducted to demonstrate proof of concept [2a], yielded extremely positive results showing exceptional improvement in vision for children with very dense amblyopia. This surprising result demonstrated that children with very poor vision could see and respond to the visual display with their amblyopic eye. Moreover, the significant improvement in vision over a relatively short period of time (6 weeks) compared to traditional occlusion therapy (several months), suggests that the neurology of amblyopia is not time-dependent. The follow-on study [2b] provided further indication of this as dramatic improvement in VA was observed after only two sessions (one hour of total treatment). However, although vision improved in 17/19

patients, the degree of improvement was variable, suggesting that children respond differently to the treatment as in traditional patching therapy. There was no pattern of response to the different types of amblyopia. This could suggest that different types of amblyopia exist, rather than the traditional classification currently used. In two of the case studies VEP measurement was applied as an objective means of verifying the subjective VA scores. However, although the first study [3a] of one patient showed a correlation between the increase in vision and the response in the brain, this was not replicated in the Nottingham study [2c] and the method of testing was poorly tolerated by the four children who had it carried out.

The Glasgow studies [3] were all conducted using the Cy-Visor headset. The pilot case study [3b] verified acceptance and reliability of the Cy-Visor headset as an alternative display, despite the need for a reclined patient posture and adult supervision required to hold the headset in place. VEPs measures were never implemented in the Glasgow studies [3b] due to availability of equipment. The Glasgow treatment study corroborated the findings of study [2a] with a larger sample of occlusion treatment failures and/or refusers. Statistical analysis of change in VA, tracked over time, verified the rapid effectiveness of I-BiT™ treatment: No significant change in VA occurred after three sessions (Waddingham et al., in preparation) or four sessions (Cleary et al., in preparation) indicating that the treatment effect occurs within two hours of total treatment time or less.

Despite differences between these studies having used different display devices, in studies applied by different research teams at different clinic locations, the overall pattern of results are similar. Examination of the proportional improvement figures shows an average of 32%-42% across all studies, with a range of 11%-92% for individual patients. The variability in effectiveness may be due to individual differences in patient conditions individual circumstances: the children had a range of different causes of their amblyopia (squint and anisometropia), a wide range of initial vision (6/15 - 6/120) and, at 5-10 years of age were older than generally considered ideal for occlusion treatment. Some of these patients had previously failed to improve with occlusion treatment, yet displayed improvement in vision using the I-BiT™ system.

8. CONCLUSIONS

We have developed a demonstrator that shows how VR technology can be used for binocular interactive treatment of amblyopia (lazy eye). Our clinical case studies provide encouraging results. Patients were keen to use the system (only 2/39 children did not want to use it) and the rapid improvement in VA from the first treatment session provided immediate positive feedback to children and parents. Moreover, as treatment effectiveness appears to occur in under 2 hours, this method of treatment would not require extensive clinic visits over long periods as initially feared.

Treatment response was variable. For some patients, I-BiT™ treatment alone was sufficient to improve vision to a satisfactory level where no further treatment was required (Cleary et al., submitted). In other patients, residual amblyopia remained and VA was further improved with traditional amblyopia treatment such as occlusion patching (Waddingham et al., 2006). Further work is required to determine when and how I-BiT™ treatment should be applied but on the basis of our case studies, we would suggest that it may be offered as a stand-alone secondary treatment or as a first-step primary treatment to bring VA up to a level from which other amblyopia treatment methods may be continued. It is hoped that an initial improvement in VA will create a positive relationship between patients (parents) and clinicians and thus improve continued treatment compliance.

I-BiT™ treatment worked more quickly than anticipated and not in the pattern expected. This raises some questions regarding the underlying neurology of amblyopia treatment. Rapid increase in VA of the amblyopic eye suggests that there is not enough time for cell growth to take place. We consider that this treatment method is enabling reactivation of dormant neural pathways instead. It follows that, if this is the case, then amblyopia treatment may not be restricted to the critical period of brain development (under 8 years of age) and therefore may be applicable to older children and adults. Certainly, there is interest from the adult amblyopia population to further investigate this: in response to a recent news item describing the I-BiT™ system (Mitchell, 2006), we have received over 200 requests from adults seeking treatment.

This is an exciting research area in its infancy. One of the challenges for further development is design and evaluation of visual content to provide stimulation for maximum treatment effectiveness that is attractive to all patients.

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